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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/610,313	07/05/2000	Susan Barnett	PP01631.101	4221

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	
MAIL DATE	**DELIVERY MODE**
03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/610,313	Applicant(s) BARNETT ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 March 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *08 March 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *48-51*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1-40 and 43-47*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's arguments against priority have already been addressed in the ofifce action mailed on 10/5/06. Thus the rejection remains for the reasons of record.
In view of the lengthy prosecution history the majority of applicant's argument have already been addressed in prior office actions mailed on 10/5/06, 2/15/06, and 6/14/04. The examiner will address only the new arguments presented by applicant.
In response to applicant's argument that the examiner has ignored both structural and functional limitations, the argument is not found persuasive because "immunogenic" is a general function of almost all polypeptides and the claimed invention embraces a nucleic acid encoding an HIV Pol polypeptide having at least one Pol activity. It is acknowledged that the goal of the invention is an improvement of immunogenicity relative to the native expression cassette (pages 78-80). The specification provides prophetic examples of the claimed invention. The art of record is absent for determining whether or not a nucleotide sequence encoding Pol polypeptide with codons found in highly expressed human genes results in improved immunogenicity. Thus, the skilled artisan would have to further experiment with the genus of expression cassettes to determine which expression cassettes contain an improved immunogenicity over native expression cassettes. In view of the prophetic examples and the lack of guidance in the art, there is no structure/function correlation between SEQ ID NOs: 30-32 and a genus of expression cassettes comprising a nucleotide sequence encoding an immunogenic HIV Pol, wherein the immunogenic HIV Pol has a clear improvement of immunogenicity over expression cassettes comprising native HIV Pol nucleotide sequences.
In response to applicant's argument that the number of amino acid substitutions is nowhere near the number alleged in the Final Rejection, the argument is not found persuasive because the calculation was based on the formula used in example N of the enablement training material (See http://www.uspto.gov/web/offices/pac/dapp/1pecba.htm#7n). The asserted statement is not supported by any evidence of record. NOTE: this calculation is just to show that the breadth of the claimed genus of nucleotide sequences is very large and the prior art of record is absent for a skilled artisan substituting up to 82 amino acids in an 819 amino acid sequence
In response to applicant's argument that the claimed invention is only directed to an HIV Pol polypeptide that elicitis a Pol-specific immune response and are not directed to any HIV Pol polypeptide (e.g., Pol polypeptides having RT and INT enzymatic activity), the argument is not found persuasive because the claims do not exclude an HIV Pol having wild type activity. The reference by applicant to WO 00/39302 (Ref B93) is moot because the claims are broader than a nucleic acid encoding an immunogenic HIV Pol that does not exhibit wild type Pol function(s).
In response to applicant's argument that the meaning attributed by the examiner is not the meaning as set forth in the specification or the meaning of the term to one of skill in the relevant art, the argument is not found persuasive because limitations in the specification are not read into the claims. There is no evidence of record to support applicant's assertion the definition "an HIV Pol that elicits a Pol-specific immune response" would apparent to one of skill in the relevant art. Furthermore, the claims have "comprising" language which would also not limit the polynucleotide to the definition asserted by applicant. Applicant argues that the specification indicates that HIV Pol can lack enzymatic function but still retain their Pol-specific immunogenicity (pages 36 and 73). However, on pages 36 and 73, the specification does not specifically discuss deleting enzymatic function, it only disccusses modifying other regions of the protein (page 36) and some instances inactivating RT and INT function (page 73). The specification further discusses making a nucleotide encoding Pol having wild type Pol activty (page 34).
In response to applicant's argument that written description does not require description of the sequence of a known molecule and that literature available at the time of filing must be considered in determining the adequacy of the written description (Falkner V. Inglis), the argument is not found persuasive because the sequences in the expression cassettes are not known molecules. A prior art search of the sequences indicates that sequences with at least 90% sequence identitiy to SEQ ID NOs: 30-32 with a desired biological activity (improved immunogenicity over native expression cassettes) were not known. There is nothing of record to indicate that modifying a Pol sequence with codons used in highly expressed human genes was known to the skilled artisan.
In response to applicant's argument that the Declaration of Dr. Donnelly (item 17) filed on 12/27/02 establishing that it was well known in the art that immunogenicity of HIV Gag polypeptides does not correlate with a core structure, the argument is not found persuasive because Dr. Donnelly does not discuss the art of record. The published article cited in the Declaration was previously addressed in a prior office action mailed on 11/28/03 Furthermore, stating that methods of making and testing Pol immunogenicity were well known in the art at the time of filing does not indicate that the applicant had possession of the claimed genus of expression cassette. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) and Fiers v. Revel, 984 F.2d at 1169, 25 USPQ2d at 1605; Amgen, 927 F.2d at 1206, 18 USPQ2d at 1021.
In response to applicant's argument that the examiner has admitted on the record that the specifciation provides written description of the claimed invention, the argument is not found persuasive because upon further consideration (the expression cassettes will provide a clear improvement of immunogenicity over native expression cassettes and prophetic working examples) and reasons of record, the examiner has changed his opinion.
In response to applicant's argument that possession of a genus is not determined by the amount of testing required and the specification provides written description for every member of the claimed genus be it 2 or 2 billion, the argument is not found persuasive because the skilled artisan would be required to further experiment to determine if a polynucleotide having 90% identity to SEQ ID NO: 30-32 has the desired biological activity. On page 78-80, applicant asserts that the expression cassettes will provide a clear improvement of immunogenicity relative to native expression cassetes, but does not provide any factual evidence to support the assertion. The art of record is absent for determining whether modiyfing a nucleic acid encoding Pol polypeptide with codons found in highly expressed human genes results in improved immunogenicity.
In response to applicant's argument that in view of opinion the in Capon v. Eshhar, the specification provides written description for the claimed invention, the argument is not found persuasive because while it is acknowledged that not every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, the species embraced by the genus is not sufficiently demonstrated to charaterzie the claimed genus of expression cassettes. The pol sequences are different than known pol sequences because the coding sequences of the claimed sequences were modified to be comparable to codon usage found in highly expressed human genes. A search of the sequences in the public databaess indicates that there is no known sequences with at least 90% sequence identity to SEQ ID NOs: 30-32. The working examples in the instant specification are prophetic. The applicant asserts tha the the

expression cassettees will provide a clear improvement of immunogenicity relative to the native expression cassettes (page 78-80).
In response to applicant's argument that reduction to practice is not required to satisfy the written description, the argument is not found persuasive because while it is acknowledged that the reduction to practice is not required to satisfy written description, the specification should provide sufficient guidance for how to make the claimed genus and disclose a correlation between the structure of the polynucleotides and desired biological activity (See Written Description Examination guidelines were published on January 5, 2001 (66 FR 1099) and are available at http://www.uspto.gov/web/menu/current.html#register.). In view of the specification not providing sufficient guidance to support the claimed genus of polynucleotides for the reasons set forth in prior office actions, one skilled in the art would recognize from the disclosure that applicant was not in possession of the claimed genus of polynucleotides.
In response to applicant's argument against the references cited in the enablement do not support the enablement rejection, the argument is not found persuasive for the reasons of record. See office action mailed on 10/5/06. There is no evidence of record teaching that it was routine to substitute up to 82 amino acids of an 892 amino acid sequence and observe a desired biological activty. Furthermore, there is no evidence of record teaching how to make and use a nucleic acid encoding Pol polypeptdies with codons found in highly expressed human genes results in clear improved immunogenicity over native nucleotide sequence encoding HIV pol. There is nothing in the claims that excludes an HIV Pol polypeptide having a Pol activity of a functional Pol protein, including immunogenicity. The description of an immunogenic composition in the specification is a general description of any polypeptide and the specification does not teach how to make and use the claimed invention wherein the polynucleotide has a clear improvement of immunogenicity relative to a native HIV Pol polypeptide.
In response to applicant's argument that it is not undue experimentation to make and use the genus of polynucleoides since it is routine to make the claimed genus, the argument is not found persuasive for the reasons of record. See office action mailed on 10/5/06. In addition, there is no evidence of record to support the assertion that it was routine to make and use a polynucleotide having codons found in highly expressed human genes, wherein expression of the polypeptide encoded by the polynucleotide has a clear improvement of immunogenicity relaive to the native expression cassettes.
In response to applicant's argument reasserting that the Delcarations of record indicate that the specifiction provides enablement for the claimed invention, the argument is not found persuasive for the reasons of record. See office actions mailed on 11/28/03.
Applicant's argument against the provisional ODP have already been addressed in a previous office action and the rejections remain for the reasons of record. See office action mailed on 10/5/06. NOTE: the co-pending application has been allowed and the issue fee has been paid.